

In the claims:

*Please amend claims 1, 6, 43, 44, and 49.*

*Please cancel claims 5, 13-16, 21, 23-27, 31-38, 47, and 48.*

*Please add new claims 50-68.*

1. **(Currently amended)** A recombinant fusion peptabody, which binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3, and or ErbB-4, comprising:

(a) a portion of a cartilage oligomer matrix polypeptide which is capable of oligomerizing;

(b) a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE, YSFEDL, YSFEDLY, YSFEDLYR, and YSFEDLYRR and for increasing protein production located at the N terminus of the peptabody portion of the cartilage oligomer matrix polypeptide;

(c) a portion of a hinge region of an immunoglobulin polypeptide located at the C terminus of the portion of the cartilage oligomer matrix polypeptide; and

(d) an epidermal growth factor receptor ligand which can bind to the epidermal growth factor receptor, located at the C terminus of the hinge region,

wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor.

2. **(Canceled)**

3. **(Canceled)**

4. **(Previously presented)** The recombinant fusion peptabody of claim 1, wherein said recombinant fusion peptabody is multimeric.

5. **(Canceled)**

6. **(Currently amended)** The recombinant fusion peptabody of claim 1, wherein said epidermal growth factor receptor ligand is selected from the group consisting of:

(a) an epidermal growth factor polypeptide or receptor binding fragments thereof ~~or variants thereof~~,

(b) a growth blocking peptide or receptor binding fragments thereof ~~or variants thereof~~,

(c) a TGF alpha polypeptide or receptor binding fragments thereof ~~or variants thereof~~,

(d) a plasmocyte spreading peptide or receptor binding fragments thereof ~~or variants thereof~~,

(e) a paralytic peptide or receptor binding fragments thereof ~~or variants thereof~~,

(f) a cardioactive peptide or receptor binding fragments thereof ~~or variants thereof~~,

(g) an amphiregulin polypeptide or receptor binding fragments thereof ~~or variants thereof~~,

(h) a heparin-binding epidermal growth factor-like polypeptide or receptor binding fragments thereof ~~or variants thereof~~,

(i) a betacellulin polypeptide or receptor binding fragments thereof ~~or variants thereof~~,  
and or

(j) a viral EGF-like polypeptide or receptor binding fragments thereof ~~or variants thereof~~.

7. **(Currently amended)** The recombinant fusion peptabody of claim 6, wherein said epidermal growth factor receptor ligand is present in its full-length sequence. ~~sequences.~~

8. **(Previously presented)** The recombinant fusion peptabody of claim 1, further comprising a polyhistidine tag sequence.

9. **(Previously presented)** The recombinant fusion peptabody of claim 1, further comprising at least one effector region.

10. **(Previously presented)** The recombinant fusion peptabody of claim 9, wherein the effector region comprises a cytotoxin or a detection moiety.

11. **(Canceled)**

12. **(Previously presented)** The recombinant fusion peptabody of claim 10, wherein said detection moiety is fluorescent.

13-16. **(Canceled)**

17. **(Previously presented)** A pharmaceutical composition comprising the recombinant fusion peptabody of claim 1, and a pharmaceutically acceptable carrier.

18-27. **(Canceled)**

28. **(Previously presented)** A kit for treating cancer characterized by expression of an epidermal growth factor receptors selected from the group consisting of ErbB1, ErbB3, and ErbB4, in a human patient, said kit comprising the recombinant fusion peptabody of claim 1 and/or instructions for administering the recombinant fusion peptabody to the human patient for the treatment of cancer.

29. **(Previously presented)** The kit of claim 28, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group consisting of a chemotherapeutic agents, an anti-epidermal growth factor receptors antibody, a radioimmunotherapeutic agents, and combinations thereof.

30. **(Previously presented)** A kit for diagnosing cancer characterized by expression of an epidermal growth factor receptors selected from the group consisting of ErbB1, ErbB3, and ErbB4, in a human patient, said kit comprising the recombinant fusion peptabody of claim 10, and instructions for use.

31-40. **(Canceled)**

41. **(Previously presented)** An isolated peptide enhancer sequence comprising an amino acid sequence selected from the group consisting of: YSFE, YSFEDL, YSFEDLY, YSFEDLYR, YSFEDLYRR, a molecular chimera thereof, and variants thereof.

42. **(Previously presented)** A recombinant protein comprising the enhancer peptide of claim 41.

43. **(Currently amended)** A recombinant fusion peptabody, which binds to the epidermal growth factor receptor ErbB-1 comprising:

(a) ~~a portion of a~~ human cartilage oligomer matrix polypeptide comprising amino acid residues 16 to 64 of SEQ ID NO: 1;

(b) a peptide enhancer sequence for increasing protein production, located at the N terminus of the ~~peptabody portion of the cartilage oligomer matrix polypeptide~~ and having a sequence selected from the group consisting of YSFE, YSFEDL, YSFEDLY, YSFEDLYR, and YSFEDLYRR;

(c) a portion of a hinge region of an immunoglobulin polypeptide comprising amino acid residues 65 to 83 of SEQ ID NO: 1, located at the C terminus of the portion of the cartilage oligomer matrix polypeptide; and

(d) an epidermal growth factor receptor ligand which binds to the epidermal growth factor receptor and is located at the C terminus of the hinge region,

wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing the epidermal growth factor receptor.

44. **(Currently amended)** A monomer of a peptabody comprising

(a) a portion of a cartilage oligomer matrix polypeptide which is capable of oligomerizing;

(b) an enhancer peptide sequence having an amino acid sequence selected from the group consisting of YSFE, YSFEDL, YSFEDLY, YSFEDLYR, and YSFEDLYRR and located at the N terminus of the ~~peptabody portion of the cartilage oligomer matrix polypeptide;~~

(c) a portion of a hinge region of an immunoglobulin polypeptide located at the C

terminus of the portion of the cartilage oligomer matrix polypeptide; and

(d) an epidermal growth factor receptor ligand located at the C terminus of the hinge region, wherein the epidermal growth factor receptor ligand binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3 or ErbB-4.

45. **(Previously presented)** The monomer of claim 44, wherein said monomer forms a multimeric molecule.

46. **(Previously presented)** The monomer of claim 45, wherein the multimeric molecule is pentameric or decameric.

47. **(Canceled)**

48. **(Canceled)**

49. **(Currently amended)** An isolated and recombinant fusion peptabody, which binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3, and ErbB-4, comprising:

(a) a portion of a humanized or human cartilage oligomer matrix polypeptide which is capable of oligomerizing;

(b) a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE, YSFEDL, YSFEDLY, YSFEDLYR, and YSFEDLYRR and ~~for increasing protein production~~ located at the N terminus of the portion of the cartilage oligomer matrix polypeptide;

(c) a portion of a hinge region comprising 19 amino acids of an immunoglobulin polypeptide, located at the C terminus of the portion of the cartilage oligomer matrix polypeptide; and

(d) an epidermal growth factor receptor ligand which binds to the epidermal growth factor receptor and is located at the C terminus of the hinge region,

wherein said isolated and recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor.

50. **(New)** The recombinant fusion peptabody of claim 43, wherein said recombinant fusion peptabody is multimeric.

51. **(New)** The recombinant fusion peptabody of claim 43, wherein said epidermal growth factor receptor ligand is selected from the group consisting of:

- (a) an epidermal growth factor polypeptide or receptor binding fragments thereof,
- (b) a growth blocking peptide or receptor binding fragments thereof,
- (c) a TGF alpha polypeptide or receptor binding fragments thereof,
- (d) a plasmocyte spreading peptide or receptor binding fragments thereof,
- (e) a paralytic peptide or receptor binding fragments thereof,
- (f) a cardioactive peptide or receptor binding fragments thereof,
- (g) an amphiregulin polypeptide or receptor binding fragments thereof,
- (h) a heparin-binding epidermal growth factor-like polypeptide or receptor binding fragments thereof,
- (i) a betacellulin polypeptide or receptor binding fragments thereof, and or
- (j) a viral EGF-like polypeptide or receptor binding fragments thereof.

52. **(New)** The recombinant fusion peptabody of claim 51, wherein said epidermal growth factor receptor ligand is present in its full-length sequence.

53. **(New)** The recombinant fusion peptabody of claim 43, further comprising a poly-histidine tag sequence.

54. **(New)** The recombinant fusion peptabody of claim 43, further comprising at least one effector region.

55. **(New)** The recombinant fusion peptabody of claim 54, wherein the effector region comprises a cytotoxin or a detection moiety.

56. **(New)** A kit for treating cancer characterized by expression of ErbB1 in a human patient, said kit comprising the recombinant fusion peptabody of claim 43 and/or instructions

for administering the recombinant fusion peptabody to the human patient for the treatment of cancer.

57. **(New)** The kit of claim 56, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group consisting of a chemotherapeutic agents, an anti-epidermal growth factor receptors antibody, a radioimmunotherapeutic agents, and combinations thereof.

58. **(New)** A kit for diagnosing cancer characterized by expression of ErbB1 in a human patient, said kit comprising the recombinant fusion peptabody of claim 55, and instructions for use.

59. **(New)** A recombinant fusion peptabody, which binds to the epidermal growth factor receptor ErbB-3 or ErbB4 comprising:

(a) a human cartilage oligomer matrix polypeptide comprising amino acid residues 16 to 64 of SEQ ID NO: 1;

(b) a peptide enhancer sequence for increasing protein production, located at the N terminus of the peptabody and having a sequence selected from the group consisting of YSFE, YSFEDL, YSFEDLY, YSFEDLYR, and YSFEDLYRR;

(c) a portion of a hinge region of an immunoglobulin polypeptide comprising amino acid residues 65 to 83 of SEQ ID NO: 1, located at the C terminus of the portion of the cartilage oligomer matrix polypeptide; and

(d) an epidermal growth factor receptor ligand located at the C terminus of the hinge region,

wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing the epidermal growth factor receptor.

60. **(New)** The recombinant fusion peptabody of claim 59, wherein said recombinant fusion peptabody is multimeric.

61. **(New)** The recombinant fusion peptabody of claim 59, wherein said epidermal growth factor receptor ligand is selected from the group consisting of:

- (a) an epidermal growth factor polypeptide or receptor binding fragments thereof,
- (b) a growth blocking peptide or receptor binding fragments thereof,
- (c) a TGF alpha polypeptide or receptor binding fragments thereof,
- (d) a plasmocyte spreading peptide or receptor binding fragments thereof,
- (e) a paralytic peptide or receptor binding fragments thereof,
- (f) a cardioactive peptide or receptor binding fragments thereof,
- (g) an amphiregulin polypeptide or receptor binding fragments thereof,
- (h) a heparin-binding epidermal growth factor-like polypeptide or receptor binding fragments thereof,
- (i) a betacellulin polypeptide or receptor binding fragments thereof, and or
- (j) a viral EGF-like polypeptide or receptor binding fragments thereof.

62. **(New)** The recombinant fusion peptabody of claim 61, wherein said epidermal growth factor receptor ligand is present in its full-length sequence.

63. **(New)** The recombinant fusion peptabody of claim 59, further comprising a poly-histidine tag sequence.

64. **(New)** The recombinant fusion peptabody of claim 59, further comprising at least one effector region.

65. **(New)** The recombinant fusion peptabody of claim 64, wherein the effector region comprises a cytotoxin or a detection moiety.

66. **(New)** A kit for treating cancer characterized by expression of ErbB1 in a human patient, said kit comprising the recombinant fusion peptabody of claim 59 and/or instructions for administering the recombinant fusion peptabody to the human patient for the treatment of cancer.



67. **(New)** The kit of claim 66, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group consisting of a chemotherapeutic agents, an anti-epidermal growth factor receptors antibody, a radioimmunotherapeutic agents, and combinations thereof.

68. **(New)** A kit for diagnosing cancer characterized by expression of ErbB1 in a human patient, said kit comprising the recombinant fusion peptabody of claim 65, and instructions for use.